

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
25 July 2002 (25.07.2002)

PCT

(10) International Publication Number
WO 02/057287 A3

(51) International Patent Classification⁷: C07H 19/14,
A61K 31/7064, A61P 31/14

(21) International Application Number: PCT/US02/03086

(22) International Filing Date: 18 January 2002 (18.01.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/263,313 22 January 2001 (22.01.2001) US
60/282,069 6 April 2001 (06.04.2001) US
60/299,320 19 June 2001 (19.06.2001) US
60/344,528 25 October 2001 (25.10.2001) US

(71) Applicants (for all designated States except US): **MERCK & CO., INC.** [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US). **ISIS PHARMACEUTICALS, INC.** [US/US]; 2292 Faraday Avenue, Carlsbad, CA 92008 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **CARROLL, Steven, S.** [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US). **MACCOSS, Malcolm** [GB/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US). **OLSEN, David, B.** [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US). **BHAT, Balkrishen** [IN/US]; 2292 Faraday Avenue, Carlsbad, CA 92008 (US). **BHAT, Neelima** [IN/US]; 2292 Faraday Avenue, Carlsbad, CA 92008 (US). **COOK, Phillip Dan** [US/US]; 2292 Faraday Avenue, Carlsbad, CA 92008 (US). **ELDRUP, Anne, B.** [DK/US]; 2292 Faraday Avenue, Carlsbad,

CA 92008 (US). **PRAKASH, Thazha, P.** [IN/US]; 2292 Faraday Avenue, Carlsbad, CA 92008 (US). **PRHAVC, Marija** [SI/US]; 2292 Faraday Avenue, Carlsbad, CA 92008 (US). **SONG, Quanlai** [CN/US]; 2292 Faraday Avenue, Carlsbad, CA 92008 (US).

(74) Common Representative: **DURETTE, Philippe, L.**; Merck & Co., Inc., 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US).

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— with international search report

(88) Date of publication of the international search report:
10 October 2002

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: NUCLEOSIDE DERIVATIVES AS INHIBITORS OF RNA-DEPENDENT RNA VIRAL POLYMERASE

(57) Abstract: The present invention provides nucleoside compounds and certain derivatives thereof which are inhibitors of RNA-dependent RNA viral polymerase. These compounds are inhibitors of RNA-dependent RNA viral replication and are useful for the treatment of RNA-dependent RNA viral infection. They are particularly useful as inhibitors of hepatitis C virus (HCV) NS5B polymerase, as inhibitors of HCV replication, and/or for the treatment of hepatitis C infection. The invention also describes pharmaceutical compositions containing such nucleoside compounds alone or in combination with other agents active against RNA-dependent RNA viral infection, in particular HCV infection. Also disclosed are methods of inhibiting RNA-dependent RNA polymerase, inhibiting RNA-dependent RNA viral replication, and/or treating RNA-dependent RNA viral infection with the nucleoside compounds of the present invention.

WO 02/057287 A3

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 02/03086

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07H19/14 A61K31/7064 A61P31/14

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07H A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 94 05687 A (UNIV BIRMINGHAM ;WELLCOME FOUND (GB); MILLER JOHN ALLEN (GB); YOUN) 17 March 1994 (1994-03-17) abstract page 4	1,12
A	Y. MURAI ET AL.: "A synthesis and an X-ray analysis of 2'-C-, 3'-C- and 5'-C-methylsangivamycins" HETEROCYCLES, vol. 33, 1992, pages 391-404, XP008004758 page 391 -page 394	1

☐ Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

*** Special categories of cited documents :*****A*** document defining the general state of the art which is not considered to be of particular relevance***E*** earlier document but published on or after the international filing date***L*** document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)***O*** document referring to an oral disclosure, use, exhibition or other means***P*** document published prior to the international filing date but later than the priority date claimed***T*** later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention***X*** document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone***Y*** document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.***&*** document member of the same patent family

Date of the actual completion of the international search

20 June 2002

Date of mailing of the international search report

01/07/2002

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

de Nooy, A

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 02/03086

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9405687	A	17-03-1994	AU 4973393 A	29-03-1994
			CA 2143834 A1	17-03-1994
			EP 0658166 A1	21-06-1995
			WO 9405687 A1	17-03-1994
			JP 8504753 T	21-05-1996
<hr/>				